Defense Threat Reduction Agency
8725 John J. Kingman Road, MS
6201 Fort Belvoir, VA 22060-6201

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TECHNICAL REPORT

Functional Polymer Surfaces for Binding, Sensing and Destruction of Bioagents

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David Whitten

Prepared by:
The Regents of the University of New Mexico
1 – University of New Mexico
Albuquerque, NM 87131

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The Regents of the University of New Mexico
1 – University of New Mexico
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14. ABSTRACT The research on this project combined several different components ranging from the synthesis of unique biocidal oligomers, the study of their photophysical properties, their incorporation into films to fundamental studies of films for capture and release of bacteria, new spectroscopic and force based methods to monitor these processes and modeling of the interaction of force-separation profiles for surfaces coated with stimuli-responsive materials. Significant progress was made in all of these areas over the 1.5 years of funding provided by this grant. A new family of biocidal materials was synthesized (oliogomeric phenylene ethynylenes, OPE) which show remarkable photophysical properties, sensing potential and dark and light-activated biocidal properties. The biocidal properties of cationic phenylene ethynlene derivatves have been shown to correlate with atomic force measurements of adhesion. Modeling studies based on Density Functional Theory has been developed for the different states of thermo-responsive polymers. Additional progress has been made possible by a second, follow-on award that is still active. Collaborations initiated under this award have continued and are still active.

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HDTRA1-07-1-0036

Title: Functional Polymer Surfaces for Binding, Sensing and Destruction of Bioagents

Investigators: David Whitten, David J. Keller, Gabriel P. Lopez, Linnea Ista, John Grey, University of New Mexico; John McCoy, New Mexico Tech

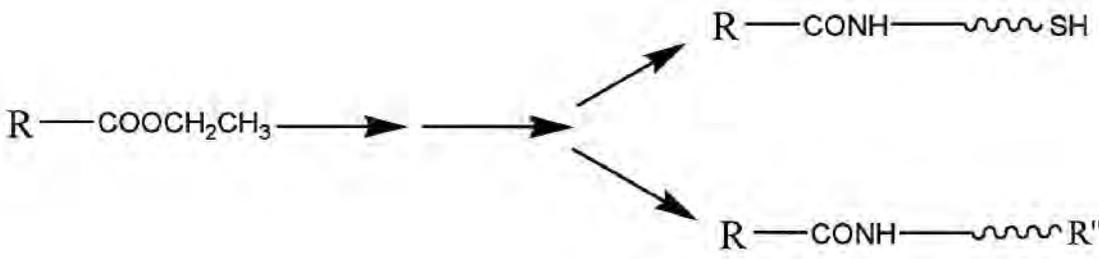
<u>Objective(s)</u> The objectives of this research are to:

1) Understand the chemical and physical reasons behind the light-activated biocidal activity of conjugated polyelectrolyte polymer films and combined smart-polymer-(stimuli-responsive polymer (SRP) conjugated polyelectrolyte blends and self-assembled monolayers (SAMs).
2) Develop a mechanistic understanding of the capture and release of bacteria, bacterial debris and biowarfare agents, using self-assembled monolayers of pure and mixed reactive agents as models.
3) Apply new spectroscopic and force-based single-particle and single-molecule methods to the reliable measurement of the thermodynamic and kinetic parameters that control adhesion and release of bacteria and other biowarfare agents to/from surfaces. Couple these investigations with modeling and sensing studies.
4) Achieve sufficient understanding of the physical and chemical basis for biocidal activity (after two years) to allow a 6.2 effort to demonstrate a CP-based decontamination system.

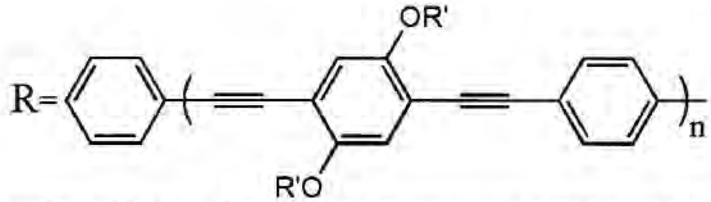
<u>Status of Effort</u> The research on this project combined several different components ranging from the synthesis of unique biocidal oligomers, the study of their photophysical properties, their incorporation into films to fundamental studies of films for capture and release of bacteria, new spectroscopic and force based methods to monitor these processes and modeling of the interaction of force-separation profiles for surfaces coated with stimuli-responsive materials. Significant progress was made in all of these areas over the 1.5 years of funding provided by this grant. A new family of biocidal materials was synthesized (oliogomeric phenylene ethynylenes, OPE) which show remarkable photophysical properties, sensing potential and dark and light-activated biocidal properties. The biocidal properties of cationic phenylene ethynlene derivatves have been shown to correlate with atomic force measurements of adhesion. Modeling studies based on Density Functional Theory has been developed for the different states of thermo-responsive polymers. Additional progress has been made possible by a second, follow-on award that is still active. Collaborations initiated under this award have continued and are still active.

<u>Accomplishments/New Findings</u>

Task 1: Preparation, characterization and photophysical studies of oligomeric conjugated polyelectrolytes (Whitten, UNM; Grey, UNM). A series of OPE were designed and synthesized for surface attachment, potential biocidal activity and combination with thermo-responsive materials in self-assembled monolayer films. The initial approach is shown in the figure below:



R'': Glass surface



n=1, 2, 3, or 4

The series with n = 1,2 and 3 was successfully synthesized, where OR' is a pendant group terminated by a trimethylammonium group. These compounds have been attached to glass surfaces of microsphere supports and planar slides. These compounds have been shown to have dark and light-activated biocidal properties against several Gram negative and Gram positive bacteria. They also have interesting photophysical properties and their sensing properties have been suggested by investigation of their photophysics in the presence and absence of negatively charged biopolymers.

Task 2: Preparation and characterization of stimuli-responsive polymer monolayers and Cells (Lopez, Ista, UNM). The goals of this task were to characterize, develop, and test two thermally responsive surfaces, poly(N-isopropyl acrylamide) (PNIPAAm) and a mixed self assembled monolayers of hexa(ethylene glycol) and alkyl thiolates (mixed SAMs). The thermally responsive behavior of PNIPAAm and the mixed SAMs make them good candidates for "smart" surfaces that can be used to controllably capture and release biowarfare agents in applications for detection and decontamination. We want to be able to understand, predict and observe the forces between simulants for biowarfare agents and the two thermally responsive surfaces. We are now able to control PNIPAAm brush synthesis and can reproducibly generate thermally responsive surfaces. The surface has been thoroughly characterized by physical and spectroscopic methods. A theoretical model for predicting both free energy and force interactions has been compared with experimental data collected from atomic force microscopy. Major accomplishments/new findings include that six model proteins we studied will not adhere to thermally responsive mixed SAM below the molecular transition. The six models proteins have different charge, shape, weight and biological functionality. To observe how protein toxins behave on the thermally responsive surface we examined, cholera toxin subunit B, as one of the six model proteins. As stated before, the model protein toxin only adheres to the mixed SAM at temperature above the thermal response. These findings together with previous findings on the reversible bioadhesion to PNIPAAm suggest that these components can be used in the design of smart surfaces that can be used to controllably capture, disable and release biowarfare agents.

Task 3: Measuring and Modeling Physical Interactions between Target Surfaces and Bacteria (Keller, UNM; Grey, UNM; McCoy, New Mexico Tech.). The main objective of this task was to understand the chemical and physical basis for adhesion and release of bacteria and biowarfare agents, using self-assembly monolayers with well-defined chemistry as models.

Four broad areas of research were proposed:

a) Directly measure adhesion forces between a bacterial cell (or other agent) and well-defined surfaces. Adhesion forces have been measured between pseudomonas aeruginaos strain PAO1 and physisorbed cationic conjugated polyelectrolyte (CPE) films. Adhesion free energy estimated. Theoretical estimates of the binding of PAO1 to CPE films as a fraction of DABCO present in mixtures with Poly NIPAAm surfaces carried out.

b) Create a map or image of adhesion force varying over a patchy, non-uniform surface. Surfaces with ATRP-grown Poly NIPAAm and OligoPEG (two classes of stimuli-responsive polymers) as well as surfaces with biocidal cationic conjugated polyelectrolyte polymers (CPE) have been individually characterized. The mixed, patterned surfaces remain to be characterized..

c) Estimate the potential free energy of interaction function between a cell (or other agent) and a spot on the surface. This has been completed not only on cells but with a variety of other surfaces. For this project the important surfaces are the CPE, Poly NIPAAm, and oligoPEG surfaces described above. The accomplishments/new findings from this task are listed below:

1. New theory relating AFM-based measurements (potentials of mean force) to simple relationships for surface on-off binding rates, equilibrium binding constants, and free energies (or surface tensions).

2. New theory relating the property statistics of a complex patchy surface to the net binding energy; how these statistics are related to properties measured by AFM or single-molecule data

3. Completion of an extensive array of AFM measurements on switchable polyNIPAAm films, and switchable oligo-ethylene glycol films.

Personnel Supported:

Faculty: David Whitten, David Keller, John Grey, Gabriel Lopez, John McCoy

Postdoctoral Fellow: Yanli Tang

Graduate Students: Keenan Dotson, Lance Edens, Brett Andrzejewski, Zhijun Zhou, Linnea Ista

Undergraduate Students: Phillip Jenks, Devon Turner

Publications:

"Understanding the Force-vs-Distance Profiles of Terminally Attached Poly(N-isopropyl acrylamide) Thin Films," Sergio Mendez, Brett P. Andrzejewski, Heather E. Canavan,

David J. Keller, John D. McCoy, Gabriel P. Lopez, and John G. Curro (Langmuir, published on Web July 28, 2009)

"Van der Waals model for phase transitions in thermoresponsive surface films," J. D. McCoy and J. G. Curro, J. Chem. Phys. 130, 194708

Yanli Tang,[†]Zhijun Zhou, Katsu Ogawa, Gabriel P. Lopez, Kirk S. Schanze, David G. Whitten, **"Synthesis, Self-Assembly and Photophysical Behavior of Oligo Phenylene Ethynylenes: From Molecular to Supramolecular Properties"**, ***Langmuir,*** *2009,* **25,** 21-25.

Yanli Tang, Zhijun Zhou, Katsu Ogawa, Gabriel P. Lopez, Kirk S. Schanze, David G. Whitten, **"Photophysics and Self-Assembly of Symmetrical and Unsymmetrical Catiomnic Oligophenylene Ethynylenes,"** ***J. Photochem. Photobiol. A: Chemistry, 2009*** **in press.**

Interactions/Transiitions:

"Comparison of AFM and Density Functional Theory Force Profiles"
K. Dotson, J. D. McCoy, D. McCoy, S. Mendez,
J. Curro, B. Andrzejewski, G. Lopez, D. Keller
Poster
March Meeting of the American Physical Society
New Orleans, Louisiana (2008).

Philadelphia ACS Meeting (DW): Light-Induced Antimicrobial Activity of Conjugated Polyelectrolytes, D. G. Whitten, T. S. Corbitt, S. Chemburu, L. K. Ista, M. Ogawa, E. Ji, D. Keller, G. P. Lopez, J. E. Fulghum, K. S. Schanze.

Presentation at the conference on Revolutionary Approaches to Hazard Mitigation in Edinburgh, Scotland (7/29/08): D.G. Whitten, T. S. Corbitt, S. Chemburu, E. Ji, J. Fulghum, G. P. Lopez, D. J. Keller, K. S. Schanze, "Light-Induced Antimicrobial Activity of Conjugated Polyelectrolytes"

Model switchable hydrophobic/hydrophilic surfaces
ELKIN conference May 2008, Santa Fe, New Mexico
Brett P. Andrzejewski, Sergio Mendez, Linnea K. Ista, Qiang Fu, Gabriel P. Lopez

Surface Force Analysis on Thermally Switchable Polymer Modified Surfaces
Chemical and Biological Defense conference, Nov. 2008, New Orleans, Louisiana
Brett Andrzejewski, Sarah McQuate, Lance Edens, Linnea Ista, David Whitten, Gabriel Lopez, and David Keller

CBD Conference, New Orleans, Nov. 08

MICROSCOPIC INTERACTION ENERGIES ON BIOCIDAL SURFACES D Keller, Department of Chemistry, University of New Mexico; Department of Chemistry, University of New Mexico; **L Edens,** Department of Chemistry, University of New Mexico; S McQuate, Department of Chemistry, University of New Mexico; K Ogawa, Department of Chemistry, University of Florida; X Zhao, Department of Chemistry, University of Florida; L Ista, Department of Chemical and Nuclear Engineering, University of New Mexico; G Lopez, Department of Chemical and Nuclear Engineering, University of New Mexico; K Schanze, Department of Chemistry, University of Florida; D Whitten, Department of Chemistry, University of Florida; MSC03 2060, 1 University of New Mexico Albuquerque, NM, 87131

Protein adhesion on the thermally responsive mixed self assembled monolayer of hexa(ethylene glycol) and dodecane thiolates
Chemical and Biological Defense conference, Nov. 2009, Houston, Texas
Brett Andrzejewski, Lance Edens, David Whitten, Gabriel Lopez, and David Keller

<u>Patent Disclosusre:</u>

Provisional patent disclosure filed with STC.UNM:
"Smart" films and Assemblies for Capture, Kill and Release of Pathogens: Dark and Light activated Antimicrobial activity of combined stimuli-respsonsive and biocidal oligomers, STC-LS-0426

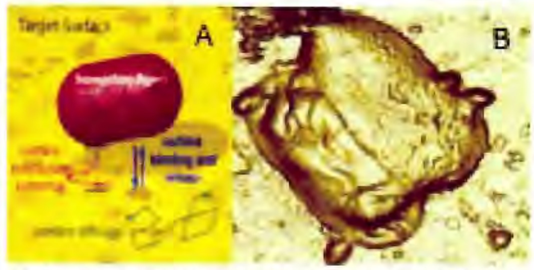
Quad Chart: Next Page

Functional Polymer Surfaces for Binding, Sensing and Destruction of Bioagents, David Whitten, University of NM, HDTRA1-07-1-0036

Description of Effort: This research: studies photo-activated biocidal activity of polymer films and stimuli-responsive polymer (SRP) films, SRP-CP blends and self-assembled monolayers (SAMs); assesses rates for capture and release of bacteria and biowarfare agents on SAMs of pure and mixed agents; applies spectroscopic and force-based single-particle and single-molecule methods to determine factors that control adhesion/release of bacteria with surfaces.

Challenges

- Develop new advanced materials for complex function
- experimental and modeling studies to understand adhesion and release



A) Basic concept of project. B) [illegible] adsorbed to a conjugated polyelectrolyte film and imaged by AFM

Benefits of Proposed Effort: The research involves novel materials, their use in defense-relevant research and their study by advanced experimental and modeling approaches. It is cross-disciplinary and involves training students in science (chemistry and biology) and engineering (chemical and biomedical engineering).

Personnel Support: Faculty (4), Professionals (2), Postdocs (1) and Graduate Student (1)

Major Goals/Milestones

FY 08 Construct and characterize SAMs composed of SRP and CP molecular components

FY 08 Carry out force measurements for attachment and release of bacteria from planar surfaces containing SAMs of SRP and CP

FY 08 Modeling for interactions of bacteria with surfaces containing SRP or CP FY 09

FY 08 Construct and characterize SAMs composed of mixed SRP and CP components

Funding Profile: 8/07 – 8/08 $402,065

PI Contact Information Prof. David Whitten, 505-277-5736, whitten@langmuir.acs.org

DEPARTMENT OF DEFENSE

DEFENSE TECHNICAL
INFORMATION CENTER
8725 JOHN J. KINGMAN ROAD,
SUITE 0944
FT. BELVOIR, VA 22060-6201
ATTN: DTIC/OCA

DEPARTMENT OF DEFENSE CONTRACTORS

ITT INDUSTRIES
ITT SYSTEMS CORPORATION
1680 TEXAS STREET, SE
KIRTLAND AFB, NM 87117-5669
ATTN: DTRIAC